	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	1	critically adj ill adj polyneuropathy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:26			0
2	BRS	L2	3	cipnp	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:24			0
3	BRS	L3	964	polyneuropathy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:26			0
4	BRS	L4	35	glucose adj regulator	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:26			0
5	BRS	L5	43637	insulin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:27			0
6	BRS	L6	76	3 same (4 or 5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 17:07			0
7	BRS	L7	76	3 same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:28			0
8	BRS	L8	6	3 same 5 same (blood adj glucose)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:49			0
9	BRS	L9	2	6558351.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:48			0
10	BRS	L10	0	3 and 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:48			0
11	BRS	L11	843	systemic adj inflammatory adj response adj syndrome	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:50			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
12	BRS	L12	6644	sirs	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:50			0
13	BRS	L13	8484	sepsis	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:51			0
14	BRS	L14	392	(11 or 12 or 13) same (4 or 5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:51			0
15	BRS	L15	8482	blood adj glucose	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:52			0
16	BRS	L16	14	14 same 15	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 14:52			0
17	BRS	L17	2	van adj den adj berghe adj greta.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/14 17:07			0

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FILE 'MEDLINE' ENTERED AT 17:12:21 14 JUL 2003

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FILE 'SCISEARCH' ENTERED AT 17:12:21 ON 14 JUL 2003
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FILE 'AGRICOLA' ENTERED AT 17:12:21 ON 14 JUL 2003

=> s critically ill polyneuropathy
L1          32 CRITICALLY ILL POLYNEUROPATHY

=> s polyneuropathy
L2       28756 POLYNEUROPATHY

=> s glucose regulator
L3         178 GLUCOSE REGULATOR

=> s l2 (p) l3
L4           1 L2 (P) L3

=> d l4 1 ibib abs

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:833142  CAPLUS
DOCUMENT NUMBER:          135:353239
TITLE:                    Critical illness neuropathy treatment with blood
                          glucose regulators
INVENTOR(S):              Van Den Berghe, Greta
PATENT ASSIGNEE(S):       Novo Nordisk A/S, Den.; K.U. Leuven R + D
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001085256      A2   20011115       WO 2001-DK287    20010430
     WO 2001085256      A3   20020221
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2001054621      A5   20011120       AU 2001-54621    20010430
     EP 1292324         A2   20030319       EP 2001-927641   20010430
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2002107178      A1   20020808       US 2001-853193   20010511
PRIORITY APPLN. INFO.:                     GB 2000-10856    A  20000505
                                           DK 2001-604      A  20010415
                                           DK 2001-605      A  20010416
                                           WO 2001-DK287    W  20010430
AB   This invention relates to a life saving medicament for critically ill
     patients and a method of treatment.  The compn. is a pharmaceutically
     effective amt. of a blood glucose regulator which is used to control the
     blood glucose level.  An examples is given of a clin. study in which the
     hypothesis that the incidence of crit. illness neuropathy can be reduced
     by more strict metab. using intensive insulin treatment from admission
     onward.
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=> d his

     (FILE 'HOME' ENTERED AT 17:12:00 ON 14 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     17:12:21 ON 14 JUL 2003
L1            32 S CRITICALLY ILL POLYNEUROPATHY
L2         28756 S POLYNEUROPATHY
L3           178 S GLUCOSE REGULATOR
L4             1 S L2 (P) L3

=> s insulin
L5        900162 INSULIN

=> s l5 (p) l1
L6             0 L5 (P) L1

=> s l5 (P) l2
L7           626 L5 (P) L2

=> s l7 (p) glucose (p) regulat?
L8            14 L7 (P) GLUCOSE (P) REGULAT?

=> duplicate remove l8
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L8
L9             6 DUPLICATE REMOVE L8 (8 DUPLICATES REMOVED)

=> s l9 not l4
L10            6 L9 NOT L4

=> d l10 1-6 ibib abs

L10  ANSWER 1 OF 6     MEDLINE
ACCESSION NUMBER:    97445365     MEDLINE
DOCUMENT NUMBER:     97445365   PubMed ID: 9300250
TITLE:               Amelioration of nerve conduction velocity following
                     simultaneous kidney/pancreas transplantation is due to the
                     glycaemic control provided by the pancreas.
AUTHOR:              Martinenghi S; Comi G; Galardi G; Di Carlo V; Pozza G;
                     Secchi A
CORPORATE SOURCE:    Department of Medicine, University of Milan, San Raffaele
                     Scientific Institute, Italy.
SOURCE:              DIABETOLOGIA, (1997 Sep) 40 (9) 1110-2.
                     Journal code: 0006777. ISSN: 0012-186X.
PUB. COUNTRY:        GERMANY: Germany, Federal Republic of
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199711
ENTRY DATE:          Entered STN: 19971224
                     Last Updated on STN: 19971224
                     Entered Medline: 19971114
AB   Diabetic   ***polyneuropathy***   is a common, disabling chronic
     complication of diabetes mellitus.  Previous studies have suggested that
     combined pancreas-kidney transplantation can ameliorate nerve conduction.
     The relative contribution of the correction of hyperglycaemia and uraemia
     on nerve function is still a matter of debate.  Nerve conduction velocity
     (NCV) was assessed before and after simultaneous pancreas and kidney
     transplantation, and before and after pancreas graft failure in five
       ***insulin***  -dependent diabetic (IDDM) patients affected by severe
     diabetic   ***polyneuropathy***   .  Sensory and motor NCV were recorded in
     five nerves and expressed as a cumulative index for each patient.
     Metabolic control was evaluated by fasting blood   ***glucose***   and
     glycosylated haemoglobin levels.  NCV index was below normal values before
     transplant: -3.8 +/- 0.7 (normal value: 0.89), improved 1 and 2 years
     after transplant: -3.1 +/- 1.3 and -2.6 +/- 0.9 (p = 0.0019), stabilised
     until pancreas failure and deteriorated to pre-transplant values 2 years
     after pancreas graft failure: -3.6 +/- 1.0 (p = 0.034).  Fasting blood
       ***glucose***   levels worsened after pancreas graft failure.  HbA1c
     levels, in the normal range during functioning pancreas graft (6.6 +/-
     0.6%), deteriorated after its failure (8.0 +/- 0.6%, p = 0.04).  Kidney
     function was preserved.  These data support a positive effect of pancreas
     transplantation per se on NCV in IDDM subjects with diabetic
       ***polyneuropathy***  , thus demonstrating that metabolic control provided
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by a self- ***regulated*** source of ***insulin*** not only halts but also ameliorates nerve fu[redacted]ion, even if ***polyneuropat[redacted]*** is advanced.

L10 ANSWER 2 OF 6 MEDLINE
ACCESSION NUMBER: 96303559 MEDLINE
DOCUMENT NUMBER: 96303559 PubMed ID: 8706071
TITLE: [Long-term treatment of diabetes with transplantation of a pancreatic segment].
Dlouhodoba lecba diabetu transplantaci segmentu pankreatu.
AUTHOR: Saudek F; Bartos V; Vanek I; Adamec M; Koznarova R; Sosna T; Boucek P; Vondrova H
CORPORATE SOURCE: Klinika diabetologie a hepatogastroenterologie IKEM, Praha.
SOURCE: CASOPIS LEKARU CESKYCH, (1996 May 29) 135 (11) 348-53.
Journal code: 0004743. ISSN: 0008-7335.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 19960919
Entered Medline: 19960911

AB BACKGROUND: Successful transplantation of the pancreas is at present the only way how to ensure on a long-term basis an almost physiological ***regulation*** of the carbohydrate metabolism in type 1 diabetics. So far it is, however, indicated mainly in patients with already advanced microangiopathy where at the same time also renal transplantation is planned and long-term experience is so far limited. The objective of the submitted paper is to report on the development of metabolic compensation and its impact on the development of microangiopathic changes in type 1 diabetics where the complete function of both grafts persisted more han five years. METHODS AND RESULTS: From a group of 34 combined transplantations of a pancreatic segment with an obliterated duct and a kidney, implemented in 1983-1988 in the Institute of Clinical and Experimental Medicine, a group of nine type 1 diabetics was followed up where the independence on exogenous ***insulin*** and haemodialyzation treatment persisted for or still persists for 5-8 years. After annual intervals the blood sugar level was examined, the intravenous ***glucose*** to tolerance test, free ***insulin*** levels, glycosylated haemoglobin, an ophthalmological and neurological examination was made, incl. the peripheral and autonomous system, and by means of a standard questionnaire the quality of life before and after transplantation was assessed. In all examined subjects normal blood sugar levels were recorded. The fasting ***insulin*** levels in transplant recipients were higher than in healthy subjects (22 vs. 10.2 microU/ml, p < 0.01) while in the course of the blood sugar curve corresponding levels were recorded. Glycosylated haemoglobin remained after 5 years quite or almost normal (4.2-7.2%). The coefficient of ***glucose*** assimilation after 5 years varied in the range from 0.7 to 1.9% min. Hypoglycaemic states were not recorded. In none of the recipients in the course of the investigation deterioration of the ophthalmological finding was observed and in three patients improvement was recorded. Symptoms of somatic ***polyneuropathy*** improved in all patients but signs of vegetative neuropathy remained unchanged. In all recipients psychic, physical and social rehabilitation as well as the general quality of life improved markedly. CONCLUSIONS: Although the group of investigated patients is so far small, the authors provided evidence that combined transplantation of the pancreas and kidney can influence in a very favourable way the quality of life and development of microangiopathic complications. As the success rate of transplantations of the pancreas in increasing and the risk of surgical complications is declining due to improving surgical techniques, the authors conclude that combined transplantation of the pancreas and kidney is at present the optimal therapeutic procedure in type 1 diabetics with chronic renal insufficiency and that indication for transplantation of the pancreas could be moved to earlier stages of diabetes when it would be possible to influence the development of diabetic microangiopathy more favourably.

L10 ANSWER 3 OF 6 MEDLINE
ACCESSION NUMBER: 93012592 MEDLINE
DOCUMENT NUMBER: 93012592 PubMed ID: 1383070
TITLE: Elevated plasma insulin-like growth factor binding protein-1 levels in type 1 (insulin-dependent) diabetic patients with peripheral neuropathy.
AUTHOR: Crosby S R; Tsigos C; Anderton C D; Gordon C; Young R J; White A

CORPORATE SOURCE: Department of Medicine, University of Manchester, Hope Hospital, Salford, UK.
SOURCE: DIABETOLOGIA, (1992 Sep) 35 (9) 868-72.
Journal code: 0006777. ISSN: 0012-186X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19960129
Entered Medline: 19921028

AB Previous studies have suggested that nerve regeneration may be defective in patients with diabetic ***polyneuropathy*** . Since ***insulin*** -like growth factor I (IGF-I) has been shown to stimulate nerve regeneration, and IGF binding protein-1 is acutely ***regulated*** by plasma ***insulin*** we have investigated the relationships between plasma IGF-I, IGFBP-1, ***glucose*** and ***insulin*** in Type 1 (***insulin*** -dependent) diabetic patients with peripheral ***polyneuropathy*** . Plasma samples were taken at hourly intervals over an 11-h period (08.00-19.00 hours) in order to characterise secretory profiles for 15 Type 1 diabetic patients (eight neuropathic and seven non-neuropathic) and eight non-diabetic control subjects. In the non-diabetic subjects, mean plasma IGF-I levels were stable throughout the 11-h period with a range of 97 micrograms/l-169 micrograms/l. In contrast, mean plasma IGFBP-1 levels declined steadily from a high level of 1.99 micrograms/l at 08.00 hours to approximately one half (0.86 microgram/l) at 15.00 hours. Comparison of areas under the curves revealed significant negative correlations between IGFBP-1 and ***glucose*** (-0.88, p = 0.01), IGFBP-1 and ***insulin*** (-0.75, p = 0.016), and IGFBP-1 and IGF-I (-0.68, p = 0.03). A significant positive correlation was found between ***insulin*** and IGF-I (+0.89, p = 0.001). The diabetic patients had markedly elevated plasma IGFBP-1 levels (area under curve, p = 0.01) and lower plasma IGF-I levels (p = 0.033) even though these patients were hyperinsulinaemic throughout the study period.(ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 4 OF 6 MEDLINE
ACCESSION NUMBER: 92043267 MEDLINE
DOCUMENT NUMBER: 92043267 PubMed ID: 1940028
TITLE: Disturbed metabolism of glucose and related hormones in familial amyloidotic polyneuropathy: hypersensitivities of the autonomic nervous system and therapeutic prevention.
AUTHOR: Ando Y; Yi S; Nakagawa T; Ikegawa S; Hirota M; Miyazaki A; Araki S
CORPORATE SOURCE: First Department of Internal Medicine, Kumamoto University Medical School, Japan.
SOURCE: JOURNAL OF THE AUTONOMIC NERVOUS SYSTEM, (1991 Jul) 35 (1) 63-70.
Journal code: 8003419. ISSN: 0165-1838.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911126

AB ***Regulation*** of ***glucose*** metabolism was evaluated by oral ***glucose*** tolerance test (OGTT) in patients with familial amyloidotic ***polyneuropathy*** (FAP). Upon oral administration of a loading dose of ***glucose*** , plasma levels of ***glucose*** , ***insulin*** and glucagon changed abnormally in all FAP patients tested. Although plasma levels of ***glucose*** and ***insulin*** in the fasted patients were within normal ranges, 33% of FAP patients showed hypoglycemia after transient hyperinsulinemia during the examination. Furthermore, another three patients showed transient hypoglycemia during their daily life. Thus, perturbed ***glucose*** metabolism should be taken into account for treating patients with FAP. The salivary glands as well as the lacrimal glands showed transient hypersecretion after chewing a gum. Histochemical analysis at autopsy revealed significant amyloid deposition in the stroma, nerves and vessels of the pancreas, but not in Langerhans islets. Similar appearance was recognized in the salivary glands. These results suggest that denervation supersensitivity might occur not only in the exocrine glands but also in the endocrine gland.

L10 ANSWER 5 OF 6 MEDLINE
ACCESSION NUMBER: 84135309 MEDLINE
DOCUMENT NUMBER: 84135309 PubMed ID: 6698835
TITLE: Neuropathy associated with diabetes mellitus in the cat.
AUTHOR: Kramek B A; Moise N S; Cooper B; Raffe M R
SOURCE: JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION, (1984 Jan 1) 184 (1) 42-5.
Journal code: 7503067. ISSN: 0003-1488.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198404
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840418

AB Distal ***polyneuropathy*** was associated with diabetes mellitus in 7 cats. Clinical signs relative to the neuropathy included a plantigrade stance, depressed patellar reflexes, hindlimb weakness, and poor postural reactions. Electromyography demonstrated reduced conduction velocity in the sciatic and ulnar nerves in 3 cats. A total of 5 cats had abatement of clinical signs following ***insulin*** therapy and blood ***glucose*** ***regulation*** or after resolution of the diabetes mellitus.

L10 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 91:442758 SCISEARCH
THE GENUINE ARTICLE: GA014
TITLE: DISTURBED METABOLISM OF GLUCOSE AND RELATED HORMONES IN FAMILIAL AMYLOIDOTIC POLYNEUROPATHY - HYPERSENSITIVITIES OF THE AUTONOMIC NERVOUS-SYSTEM AND THERAPEUTIC PREVENTION
AUTHOR: ANDO Y (Reprint); YI S; NAKAGAWA T; IKEGAWA S; HIROTA M; MIYAZAKI A; ARAKI S
CORPORATE SOURCE: KUMAMOTO UNIV, SCH MED, DEPT INTERNAL MED 1, 1-1-1 HONJO, KUMAMOTO 860, JAPAN (Reprint); KUMAMOTO UNIV, SCH MED, DEPT SURG 2, KUMAMOTO 860, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: JOURNAL OF THE AUTONOMIC NERVOUS SYSTEM, (1991) Vol. 35, No. 1, pp. 63-70.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 16
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB ***Regulation*** of ***glucose*** metabolism was evaluated by oral ***glucose*** tolerance test (OGTT) in patients with familial amyloidotic ***polyneuropathy*** (FAP). Upon oral administration of a loading dose of ***glucose*** , plasma levels of ***glucose*** , ***insulin*** and glucagon changed abnormally in all FAP patients tested. Although plasma levels of ***glucose*** and ***insulin*** in the fasted patients were within normal ranges, 33% of FAP patients showed hypoglycemia after transient hyperinsulinemia during the examination. Furthermore, another three patients showed transient hypoglycemia during their daily life. Thus, perturbed ***glucose*** metabolism should be taken into account for treating patients with FAP. The salivary glands as well as the lacrimal glands showed transient hypersecretion after chewing a gum. Histochemical analysis at autopsy revealed significant amyloid deposition in the stroma, nerves and vessels of the pancreas, but not in Langerhans islets. Similar appearance was recognized in the salivary glands. These results suggest that denervation supersensitivity might occur not only in the exocrine glands but also in the endocrine gland.

=> d his

(FILE 'HOME' ENTERED AT 17:12:00 ON 14 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 17:12:21 ON 14 JUL 2003
L1 32 S CRITICALLY ILL POLYNEUROPATHY
L2 28756 S POLYNEUROPATHY
L3 178 S GLUCOSE REGULATOR
L4 1 S L2 (P) L3
L5 900162 S INSULIN
L6 0 S L5 (P) L1
L7 626 S L5 (P) L2

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L8          14 S L7 (P) GLUCOSE (P) REGULAT?
L9           6 DUPLICATE REMOVE L8 (8 DUPLICATES REMOVED)
L10          6 S L9 NOT L4

=> s systemic inflammatory response syndrome
L11       4562 SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

=> s sirs
L12       3926 SIRS

=> s l11 or l12
L13       6511 L11 OR L12

=> s sepsis
L14     135459 SEPSIS

=> s (l13 or l14) (p) l5
L15       1454 (L13 OR L14) (P) L5

=> s l15 (p) glucoe (p) regulat?
L16          0 L15 (P) GLUCOE (P) REGULAT?

=> s l15 (p) glucose (p) regulat?
L17         71 L15 (P) GLUCOSE (P) REGULAT?

=> duplicate remove l17
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L17
L18          25 DUPLICATE REMOVE L17 (46 DUPLICATES REMOVED)

=> d l18 1-25 ibib abs

L18  ANSWER 1 OF 25  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   2002:485512  BIOSIS
DOCUMENT NUMBER:    PREV200200485512
TITLE:              IGFBP-3 inhibits insulin action.
AUTHOR(S):          Yang, S. T. (1); Shim, M. (1); Cohen, P. (1)
CORPORATE SOURCE:   (1) University of California, Los Angeles, CA USA
SOURCE:             American Zoologist, (December, 2001) Vol. 41, No. 6, pp.
                    1654. print.
                    Meeting Info.: Annual Meeting of the Society for
                    Integrative and Comparative Biology Anaheim, California,
                    USA January 02-06, 2002
                    ISSN: 0003-1569.
DOCUMENT TYPE:      Conference
LANGUAGE:           English
AB   IGFBP-3 is known to have IGF-independent actions on cell growth and
     metabolism. We found that BP-3 inhibits   ***insulin***  -stimulated
       ***glucose***   transport in rodent 3T3-L1 adipocytes. Indeed, BP-3
     inhibited   ***insulin***  -stimulated GLUT-4 translocation from the
     cytoplasm to the surface membrane. BP-3's ability to inhibit
       ***glucose***   transport in 3T3-L1 adipocytes is similar to that seen
     with TNF&alpha;, an established suspect in mediating   ***insulin***
     resistance. We found that TNF&alpha; stimulates the production and nuclear
     localization of BP-3 in these cells. The inhibitory action of TNF&alpha;
     on   ***glucose***   transport was partially blocked by concomitant
     treatment with BP-3 antisense oligos, suggesting that BP-3 may be a
     mediator of TNF&alpha;-induced   ***insulin***   resistance. Our lab had
     previously discovered that BP-3 binds the nuclear receptor RXR, the
     obligate partner for PPAR&gamma;, and modulates its transcriptional
     acitivity. Because TNF&alpha; is known to induce   ***insulin***
     resistance by antagonizing PPAR&gamma; activity, we decided to investigate
     whether BP-3 would have similar effects. BP-3 does indeed inhibit
     PPAR&gamma; transcriptional acitivity in a dose-dependent manner, as well
     as PPAR&gamma;-stimulated adipogenesis and   ***glucose***   transport. To
     assess the in vivo effects of BP-3 on   ***insulin***   action, we
     employed euglycemic   ***insulin***   clamps in Sprague-Dawley male rats.
     Acute BP-3 treatment for 3 hours antagonized   ***insulin***  's ability
     to suppress hepatic   ***glucose***   production. Chronic treatment for 7
     days also prevented   ***insulin***  's inhibition of hepatic
       ***glucose***   production as well as peripheral   ***glucose***
     utilization. The exact mechanism by which BP-3 antagonizes   ***insulin***
     action are yet uncharacterized but may involve interference of
       ***insulin***   signaling. BP-3 may be an important   ***regulator***   of
       ***insulin***   action in   ***insulin***   resistant and catabolic states
     such as   ***sepsis***   and starvation.
```

L18 ANSWER 2 OF 25 MEDLINE DUPLICATE
ACCESSION NUMBER: 2001692766 MEDLINE
DOCUMENT NUMBER: 21603258 PubMed ID: 11735664
TITLE: Acute renal failure in children: aetiology and management.
AUTHOR: Filler G
CORPORATE SOURCE: Department of Paediatrics, Division of Paediatric Nephrology, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada.. filler@cheo.on.ca
SOURCE: PAEDIATRIC DRUGS, (2001) 3 (11) 783-92. Ref: 68
Journal code: 100883685. ISSN: 1174-5878.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011213
Last Updated on STN: 20020125
Entered Medline: 20020115

AB This review evaluates the various causes and management of acute renal failure (ARF) in children. ARF is defined as an abrupt decline in the renal ***regulation*** of water, electrolytes and acid-base balance, and continues to be an important factor contributing to the morbidity and mortality of critically ill infants and children. The common causes of ARF in children include acute tubular necrosis secondary to various causes (including congestive heart failure and ***sepsis***), haemolytic uremic syndrome, and glomerulonephritis and urinary tract obstruction. Ischaemia, toxins (including drugs) as well as primary parenchymal disease, have to be considered and ARF can also be a complication of systemic disease. The basic principles of management are avoidance of life-threatening complications, maintenance of fluid and electrolyte balance, and nutritional support. Only a few patients require specific management of the underlying disorder, although it is important to diagnose these conditions. Knowledge about the use of drugs for the prevention of ARF is scarce. Mannitol, low-dose dopamine, calcium channel antagonists, atrial natriuretic peptide and albumin have been evaluated and, where possible, meta-analyses are cited. Mannitol treatment appears to be warranted prophylactically after paediatric renal transplantation. Albumin infusion can reverse prerenal ARF in children with nephritic syndrome. For treatment of the complications of hyperkalaemia and volume overload, salbutamol, ***insulin*** and ***glucose*** infusion and diuretics such as furosemide and sodium bicarbonate, are discussed. All of the major dialysis modalities (peritoneal dialysis, haemodialysis and continuous haemofiltration) can be used to provide equivalent solute clearance and ultrafiltration. The indication for, and the choice of the modality depend on the patient requirements and on local resources, and should involve the care of a paediatric nephrologist. Peritoneal dialysis requires minimal equipment and infrastructure, is easy to perform and remains the favoured modality of renal replacement therapy in children. However, continuous haemofiltration is an excellent alternative to peritoneal dialysis in patients with ARF and severe fluid overload. Dialysis remains the most important tool to bridge the time needed for recovery of renal function. There is increasing evidence that more intense use of dialysis may improve the overall prognosis.

L18 ANSWER 3 OF 25 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001110348 MEDLINE
DOCUMENT NUMBER: 20567166 PubMed ID: 11115349
TITLE: Signaling mechanisms of altered cellular responses in trauma, burn, and sepsis: role of Ca2+.
AUTHOR: Sayeed M M
CORPORATE SOURCE: Department of Surgery, Loyola University Medical Center, 2160 S First Ave, Maywood, IL 60153, USA.. msayeed@luc.edu
CONTRACT NUMBER: ROI-GM53235 (NIGMS)
ROI-GM56865 (NIGMS)
SOURCE: ARCHIVES OF SURGERY, (2000 Dec) 135 (12) 1432-42. Ref: 118
Journal code: 9716528. ISSN: 0004-0010.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322
Entered Medlin[redacted]20010202

AB Alterations in cellular responses in various organ systems contribute to trauma-, burn-, and ***sepsis*** -related multiple organ dysfunction syndrome. Such alterations in muscle contractile, hepatic metabolic, and neutrophil and T-cell inflammatory-immune responses have been shown to result from cell-signaling modulations and/or impairments in the respective cell types. Altered Ca(2+) signaling would seem to play an important role in the myocardial and vascular smooth muscle contractile dysfunction in the injury conditions; Ca(2+)-linked signaling derangement also plays a crucial role in ***sepsis*** -induced altered skeletal muscle protein catabolism and resistance to ***insulin*** -mediated ***glucose*** use. The injury-related increased hepatic gluconeogenesis and acute-phase protein response could also be caused by a pathophysiologic up- ***regulation*** of hepatocyte Ca(2+)-signal generation. The increased oxidant production by neutrophil, a potentially detrimental inflammatory response in early stages after burn or septic injuries, seems to result from an up- ***regulation*** of both the Ca(2+)-dependent as well as Ca(2+)-independent signaling pathways. The injury conditions would seem to cause an inappropriate up- ***regulation*** of Ca(2+)-signal generation in the skeletal myocyte, hepatocyte, and neutrophil, while they lead to a down- ***regulation*** of Ca(2+) signaling in T cells. The crucial signaling derangement that causes T-cell proliferation suppression seems to be a decrease in the activation of protein tyrosine kinases, which subsequently down- ***regulates*** Ca(2+) signaling. The delineation of cell-signaling derangements in trauma, burn, or ***sepsis*** conditions can lead to development of therapeutic interventions against the disturbed cellular responses in the vital organ systems.

L18 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 2000:260159 BIOSIS
DOCUMENT NUMBER: PREV200000260159
TITLE: The metabolic response to injury and sepsis.
AUTHOR(S): Kreymann, K. G. (1); Wolf, M.
CORPORATE SOURCE: (1) Medizinische Kernklinik und Poliklinik, Universitaets-Krankenhaus Eppendorf, Martinistrasse 52, D-20246, Hamburg Germany
SOURCE: Intensiv- und Notfallbehandlung, (2000) Vol. 25, No. 1, pp. 4-19. print..
ISSN: 0947-5362.
DOCUMENT TYPE: Article
LANGUAGE: German
SUMMARY LANGUAGE: English; German

AB A rapid loss of muscle mass, ***insulin*** -resistant hyperglycemia and a pronounced hypermetabolism are the most important metabolic alterations induced by the ***systemic*** ***inflammatory*** ***response*** ***syndrome*** . Although often labeled as autocannibalism, they are the result of a reasonable evolutionary process due to the fact that in history critical illness was mostly associated with reduced food ingestion and all substrates necessary for the healing process had to be recovered from endogenous resources. The aim of the metabolic adaption to generalized inflammation is to provide amino acids for the augmented protein synthesis, to satisfy the carbohydrate demand of ***glucose*** -dependant tissues and to furnish enough energy under the condition of hypermetabolism. These ends are accomplished by increased proteolysis in muscle cells, enhanced gluconeogenesis in the liver and increased lipolysis of stored triglycerides. For all three substances, the appearance rate exceeds the utilization, which reflects an all-or-nothing reaction of the organism with the goal of a prompt recovery and return to food ingestion. Under these conditions, the metabolic ***regulation*** has to be uncoupled from exogenous substrate supply. In consequence, a general reversal of the metabolic situation by exogenous provision of nutritive agents is not possible. However, although the most important clinical following, the loss of muscle mass and other proteins, can not be completely prevented, a substrate-oriented nutritional approach can at least significantly reduce it.

L18 ANSWER 5 OF 25 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998240815 MEDLINE
DOCUMENT NUMBER: 98240815 PubMed ID: 9581683
TITLE: Interleukin 1beta and interleukin 6, but not tumor necrosis factor alpha, inhibit insulin-stimulated glycogen synthesis in rat hepatocytes.
AUTHOR: Kanemaki T; Kitade H; Kaibori M; Sakitani K; Hiramatsu Y; Kamiyama Y; Ito S; Okumura T

CORPORATE SOURCE: First Department of Surgery, Kansai Medical University, Moriguchi, Osa[redacted] Japan.
SOURCE: HEPATOLOGY, (1998 May) 27 (5) 1296-303.
Journal code: 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980519

AB Recent evidence indicates that inflammatory cytokines are involved in changes of blood ***glucose*** concentrations and hepatic ***glucose*** metabolism in infectious diseases, including ***sepsis*** . However, little is known regarding how cytokines interact with glucoregulatory hormones such as ***insulin*** . The objective of the present study is to investigate if and how cytokines influence ***insulin*** -stimulated glycogen metabolism in the liver. Interleukin 1beta (IL-1beta) and interleukin 6 (IL-6) markedly inhibited the increase of glycogen deposition stimulated by ***insulin*** in primary rat hepatocyte cultures; however, tumor necrosis factor alpha had no effect. Labeling experiments revealed that both cytokines counteracted ***insulin*** action by decreasing [14C]- ***glucose*** incorporation into glycogen and by increasing [14C]-glycogen degradation. Furthermore, it was discovered that IL-1beta and IL-6 inhibited glycogen synthase activity and, in contrast, accelerated glycogen phosphorylase activity. In experiments with kinase inhibitors, serine/threonine kinase inhibitor K252a blocked IL-1beta- and IL-6-induced inhibitions of glycogen deposition, as well as glycogen synthase activity, whereas another kinase inhibitor staurosporine blocked only IL-6-induced inhibition. Tyrosine kinase inhibitor herbimycin A blocked only IL-1beta-induced inhibition. These results indicate that IL-1beta and IL-6 ***regulate*** ***insulin*** -stimulated glycogen synthesis through different pathways involving protein phosphorylation in hepatocytes. They may mediate the change of hepatic ***glucose*** metabolism under pathological and even physiological conditions by modifying ***insulin*** action in vivo.

L18 ANSWER 6 OF 25 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97095350 MEDLINE
DOCUMENT NUMBER: 97095350 PubMed ID: 8940683
TITLE: Energy substrate metabolism during stress.
AUTHOR: Sugimoto H
CORPORATE SOURCE: Department of Traumatology and Critical Care Medicine, Osaka University School of Medicine, Suita, Japan.
SOURCE: NIPPON GEKA GAKKAI ZASSHI. JOURNAL OF JAPAN SURGICAL SOCIETY, (1996 Sep) 97 (9) 726-32. Ref: 17
Journal code: 0405405. ISSN: 0301-4894.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19980206
Entered Medline: 19961231

AB Energy substrate metabolism during stress is characterized by increased REE (resting energy expenditure), hyperglycemia, hyperlactatemia and protein catabolism. This stress-induced hypermetabolic responses are closely related to increased secretion of neurohormonal and cytokine mediators. The ***insulin*** resistance hyperglycemia has been called "stress diabetes" or "surgical diabetes". ***Glucose*** disposal has been thought to be impaired in this condition. However, ***glucose*** uptake in most tissue is non- ***insulin*** mediated. Recent studies showed ***glucose*** uptake elevated in ***sepsis*** or TNF infusion. ***Insulin*** - ***regulatable*** ***glucose*** transporter (GLUT4) is present only in muscle, heart and adipose tissues. It was demonstrated that ***insulin*** binding to membrane receptors in these tissues was intact. This hyperglycemia in stress diabetes results from a postreceptor mechanism. Stress hyperlactatemia is thought to be caused by decreased pyruvate dehydrogenase activity rather than tissue hypoperfusion. Hyperlactatemia may promote gluconeogenesis. ***Glucose*** is a essential energy substrate in some tissues such as brain, erythrocyte and leukocyte. Hyperglycemia may be viewed as a beneficial response during stress.

L18 ANSWER 7 OF 25 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96255323 MEDLINE
DOCUMENT NUMBER: 96255323 PubMed ID: 8689277
TITLE: Alterations in calcium signaling and cellular responses in septic injury.
AUTHOR: Sayeed M M
CORPORATE SOURCE: Department of Physiology, Loyola University Chicago, Stritch School of Medicine, Maywood, IL, USA.
CONTRACT NUMBER: RO1GM32288 (NIGMS)
RO1GM53235 (NIGMS)
SOURCE: NEW HORIZONS, (1996 Feb) 4 (1) 72-86. Ref: 114
Journal code: 9416195. ISSN: 1063-7389.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960911
Last Updated on STN: 19970203
Entered Medline: 19960826

AB The immune and endocrine mediators that are released during ***sepsis*** (e.g., tumor necrosis factor [TNF] alpha, interleukin [IL]-1, IL-6, transforming growth factor [TGF] beta, prostaglandin [PG] E2, catecholamines, vasopressin, glucagon, ***insulin*** , and glucocorticoids) can produce inappropriate detrimental cellular responses contributing to exacerbation of septic injury. Examples of such ***sepsis*** -related inappropriate responses are: exaggerated hepatic acute-phase protein (APP) expression and release skeletal muscle ***insulin*** resistance, and suppressed T-lymphocyte proliferation. The studies discussed in this article present evidence that the generation of the ***sepsis*** -related hepatic, skeletal muscle, and T-lymphocyte responses emanate from alterations in intracellular Ca2+ (Ca2+i) homeostasis. In hepatocytes, there is indication of a ***sepsis*** -mediated increase in Ca2+ influx from the extracellular milieu leading to a sustained increase in the apparent resting cell Ca2+i concentration ([Ca2+]i) and its depressed elevation on stimulation with Ca2+-mobilizing hormones such as catecholamines and vasopressin. These Ca(2+)- related changes can affect not only the signaling pathways in which Ca2+i itself serves as a signaling component, but also the signaling systems turned on by other ***sepsis*** -induced agonists which may not be dependent on Ca2+ signaling. TGF-beta, IL-1, TNF alpha, and IL-6 activate a primarily protein kinase C (PKC)-dependent intracellular signal system for the elicitation of a normal hepatic APP response (APPR). The increased apparent basal [Ca2+]i in ***sepsis*** can hypersensitize PKC activation and thus lead to an exaggerated APPR. In the skeletal muscle, an evident increase in Ca2+ membrane flux during ***sepsis*** pointed to an increase in the basal [Ca2+]i resulting from a plausible cytokine-mediated overactivation of the voltage-sensitive Ca2+ channels. The increased basal [Ca2+]i can negatively modulate the ***insulin*** -mediated stimulation of GLUT4-dependent ***glucose*** transport despite the possibility that Ca2+i might not participate as a component in the ***insulin*** -receptor- ***regulated*** signaling pathway. Increased [Ca2+]i in skeletal myocytes can either directly promote the phosphorylation of GLUT4 or prevent its dephosphorylation, both of which effectively block ***insulin*** stimulation of ***glucose*** uptake, thereby contributing to ***insulin*** resistance. In T lymphocytes, septic injury appears to induce an attenuation in the mitogen and, thus, presumably a T-cell antigen receptor (TCR)-mediated elevation in [Ca2+]i without affecting the basal [Ca2+]i. This decrease in TCR-related Ca2+i mobilization evidently contributes to the suppression of T lymphocyte proliferation during ***sepsis*** , probably via an in vivo action of prostaglandin (PG) E2 on the T cells during ***sepsis*** . The blockade of PGE2 production after indomethacin administration to septic animals prevents alterations in both T-cell Ca2+i mobilization and proliferation. PGE2 probably acts through its second messenger, cyclic adenosine 3'5'-monophosphate, which can antagonize Ca2+i signaling in T cells.

L18 ANSWER 8 OF 25 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96046841 MEDLINE
DOCUMENT NUMBER: 96046841 PubMed ID: 7586625
TITLE: Distributed anabolic hormonal patterns in burned patients: the relation to glucagon.
AUTHOR: Nygren J; Sammann M; Malm M; Efendic S; Hall K; Brismar K;

Ljungqvist O
CORPORATE SOURCE: Department of [redacted]gery, Karolinska Hospital, St[redacted]holm, Sweden.
SOURCE: CLINICAL ENDOCRINOLOGY, (1995 Oct) 43 (4) 491-500.
Journal code: 0346653. ISSN: 0300-0664.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951205

AB OBJECTIVE: Complex changes in the anabolic ***regulators*** of metabolism occur after major injury. We have studied the time course for IGF-I and IGFBP-1 after burn injury and their relations to circulating levels of other anabolic and catabolic hormones. The hormonal patterns during the onset of ***sepsis*** were also investigated. PATIENTS: Eight patients (age 36 (6) years, mean (SEM)) with major burn injury (burn area 42 (6) %) were studied. The first 2 days since the burn were used for rehydration therapy (rehydration period), after which a complete total parenteral nutrition (TPN) period was initiated. Seven positive blood cultures, during the study period. Six of the eight survived. MEASUREMENTS: The hormonal changes determined in the morning during the first 7 days after the burn and from day 22 to 24 were investigated. The superimposed effects of ***sepsis*** were studied by normalizing all data to the day of positive blood cultures and clinical onset of ***sepsis*** . RESULTS: On admission, plasma levels of glucagon, IGFBP-1 and GH were elevated while levels of IGF-I were low. During the first week after the burn, morning levels of glucagon and ***insulin*** increased while levels of GH and IGF-I decreased. GH levels were still elevated compared to healthy subjects. Despite the increase in ***insulin*** levels, IGFBP-1 remained elevated. Three weeks after the burn injury, IGF-I levels were increased but still markedly below normal, while IGFBP-1 levels remained unchanged. Persistent elevations of ***insulin*** levels were combined with reductions in glucagon levels. Admission levels of IGFBP-1 correlated to nitrogen loss (negative nitrogen balance) during the first 24 hours after the burn ($r = 0.84$, $P < 0.05$). A correlation between negative nitrogen balance and glucagon levels was found during early catabolic period in the rehydration period (i.e. days 2-3, $r = 0.84$, $P < 0.01$). The relative change in IGFBP-1 levels in the rehydration period correlated to changes in glucagon levels (days 2-3 vs admission, $r = 0.85$, $P < 0.05$). The ***insulin*** /glucagon molar ratio correlated to the IGF-I/IGFBP-1 ratio during both the rehydration period (days 2-3, $r = 0.77$, $P < 0.05$) and the third week after the burn ($r = 0.77$, $P < 0.05$). During the most catabolic phase in the first week after the burn (TPN period) there was an inverse relation between IGF-I and IGFBP-I and glucagon ($r = 0.83$, $P < 0.05$). During the less catabolic third week after the burn, an inverse correlation was found between IGF-I and glucagon ($r = -0.83$, $P < 0.05$). ***Sepsis*** , superimposed upon the burn trauma, was associated with transient elevations in IGFBP-1 and reductions in ***insulin*** despite elevated levels of ***glucose*** and a further 50% increase in nitrogen losses. CONCLUSIONS: The present findings show that marked changes is important anabolic ***regulating*** factors occur after major burn injury. Uncoupling of the GH-IGF-I axis, and the attenuation of the inhibitory effects of ***insulin*** on IGFBP-1, both contribute to the reduction in IGF-I levels and bioavailability, factors which may play an important role in post injury metabolism. Furthermore, these data suggest that the catabolic hormones (catecholamines, cortisol and glucagon), primarily glucagon seem to be involved in the modulation of IGF-I and IGFBP-1 levels following burn injury.

L18 ANSWER 9 OF 25 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 94187636 MEDLINE
DOCUMENT NUMBER: 94187636 PubMed ID: 8139474
TITLE: Effects of systemic infusions of endotoxin, tumor necrosis factor, and interleukin-1 on glucose metabolism in the rat: relationship to endogenous glucose production and peripheral tissue glucose uptake.
AUTHOR: Ling P R; Bistrian B R; Mendez B; Istfan N W
CORPORATE SOURCE: Laboratory of Nutrition/Infection, New England Deaconess Hospital, Harvard Medical School, Boston, MA 02215.
CONTRACT NUMBER: CA 45768 (NCI)
DK 31933 (NIDDK)
DK 40492 (NIDDK)
+

SOURCE: METABOLISM: CLINICAL AND EXPERIMENTAL, (1994 Mar) 43 (3) 279-84.
Journal code: 0375267. ISSN: 0026-0495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940509
Last Updated on STN: 19940509
Entered Medline: 19940426

AB This study was performed to characterize and compare the actions of ***insulin*** on hepatic ***glucose*** production and peripheral ***glucose*** utilization during infusions of endotoxin, tumor necrosis factor (TNF), interleukin-1 (IL-1), and a combination of IL-1 and TNF in the rat. The euglycemic hyperinsulinemic clamp technique was combined with a primed-constant tracer infusion of high-performance liquid chromatography (HPLC)-purified 3H-3- ***glucose*** for estimation of whole-body ***glucose*** appearance and utilization rates; 14C-deoxyglucose (14C-DG) uptake was also measured in specific tissues following intravenous bolus administration. As expected, acute endotoxemia resulted in a significant reduction of ***glucose*** infusion during the clamp procedure (***insulin*** concentration, 100 microU/mL), suggesting decreased ***insulin*** action. Similarly, infusion of TNF decreased the rate of ***glucose*** infusion necessary to maintain euglycemia. However, differences between endotoxin- and cytokine-treated rats were noted in whole-body ***glucose*** appearance (or disappearance) rates. Whereas endotoxin infusion predominantly decreased whole-body ***glucose*** uptake, suggesting diminished utilization in skeletal muscles, cytokine infusions were associated with a measurable hepatic ***glucose*** output despite hyperinsulinemia. In contrast, both cytokine and endotoxin administration decreased the rate of 14C-DG uptake by muscle tissue. These results demonstrate that TNF, IL-1, and endotoxin can induce a state of ***insulin*** resistance when infused continuously; the results also emphasize the complexity of ***regulation*** of ***glucose*** homeostasis during infection and ***sepsis*** .

L18 ANSWER 10 OF 25 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 91114639 MEDLINE
DOCUMENT NUMBER: 91114639 PubMed ID: 1989854
TITLE: Gram-negative infection increases noninsulin-mediated glucose disposal.
AUTHOR: Lang C H; Dobrescu C
CORPORATE SOURCE: Department of Physiology, Louisiana State University Medical Center, New Orleans 70112.
CONTRACT NUMBER: GM 38032 (NIGMS)
SOURCE: ENDOCRINOLOGY, (1991 Feb) 128 (2) 645-53.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 19910329
Entered Medline: 19910304

AB Peripheral ***glucose*** uptake can occur by either ***insulin*** - or noninsulin-mediated mechanisms, and the two pathways appear to be ***regulated*** independently. Using the euglycemic hyperinsulinemic clamp technique, we have previously demonstrated that ***sepsis*** induces whole body ***insulin*** resistance. The purpose of the present study was to determine whether infection also alters noninsulin-mediated ***glucose*** uptake (NIMGU) and, if so, which tissues are affected. Studies were performed in chronically catheterized conscious rats under either basal (6 mM ***glucose*** , 30 microU/ml ***insulin***) or insulinopenic conditions to determine NIMGU. Hypermetabolic ***sepsis*** was induced by sc injections of live Escherichia coli, and 24 h later a tracer amount of [U-14C]deoxy-2- ***glucose*** was injected for the determination of the in vivo ***glucose*** metabolic rate (Rg) in selected tissues. Our results indicate that NIMGU is the predominant route of ***glucose*** disposal in both septic and nonseptic rats, accounting for 79-83% of the total rate of ***glucose*** disposal. Because the rate of whole body ***glucose*** disposal was increased by ***sepsis*** , the absolute rate of NIMGU was 46% higher in septic rats than in nonseptic animals. This increase was the result of the elevated Rg in liver, spleen, ileum,

and lung. ***Sepsis*** also increased whole body ***insulin*** -mediated ***glucose*** uptake by 88% under basal conditions, and this was due to an enhanced ***glucose*** uptake by muscle and skin. In insulinopenic animals in which the plasma ***glucose*** concentration was elevated to 17 mM, whole body ***glucose*** disposal increased by 107% in nonseptic animals, but by only 32% in septic rats. The hyperglycemic-induced increment in organ Rg was smaller in all tissues examined from septic animals. However, the absolute rate of whole body and tissue ***glucose*** utilization was not different between the two groups. These results indicate that gram-negative infection increases whole body NIMGU, which results from an enhanced rate of ***glucose*** utilization by tissues rich in mononuclear phagocytes, including the liver, spleen, ileum, and lung, but not by muscle.

L18 ANSWER 11 OF 25 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 91215893 MEDLINE
DOCUMENT NUMBER: 91215893 PubMed ID: 1850680
TITLE: Hepatic phosphofructokinase-1 activity and fructose 2,6-bisphosphate levels in patients with abdominal sepsis.
AUTHOR: Arnold J; Hamer M J; Irving M
CORPORATE SOURCE: Department of Surgery, University of Manchester, U.K.
SOURCE: CLINICAL SCIENCE, (1991 Mar) 80 (3) 213-7.
Journal code: 7905731. ISSN: 0143-5221.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199106
ENTRY DATE: Entered STN: 19910623
Last Updated on STN: 19910623
Entered Medline: 19910603

AB 1. In ***sepsis*** various processes of carbohydrate metabolism, such as hepatic gluconeogenesis and glycolysis, are altered. Phosphofructokinase-1, a key glycolytic enzyme, is controlled in the long term via ***regulation*** of synthesis and degradation of the protein itself, while in the short term it is ***regulated*** by allosteric effectors, such as fructose 2,6-bisphosphate (the most potent). In the present study hepatic phosphofructokinase-1 activity as well as phosphofructokinase-2 activity and the concentration of fructose 2,6-bisphosphate were assayed to determine if they might contribute to the derangement of carbohydrate metabolism seen commonly in ***sepsis*** . 2. The levels of glycogen and fructose 2,6-bisphosphate and the activity of phosphofructokinase-1 and phosphofructokinase-2 were determined in hepatic biopsies obtained at laparotomy from six patients with and seven patients without abdominal septic foci. 3. A significant increase in plasma lactate concentration was observed in the septic patients, whereas no significant differences in tissue glycogen content or plasma ***glucose*** concentration were seen between the groups. 4. No significant change in plasma ***insulin*** concentration was observed. However, levels of the counter- ***regulatory*** hormones (glucagon, cortisol and adrenaline) were elevated in the septic patients. 5. A 60% decrease in hepatic phosphofructokinase-1 activity was seen in the septic patients. However, no significant changes in hepatic phosphofructokinase-2 activity and fructose 2,6-bisphosphate content were observed in the septic patients. 6. The present results demonstrate that the decrease in hepatic phosphofructokinase-1 activity occurring in ***sepsis*** does not appear to reflect alterations in the concentration of fructose 2,6-bisphosphate.

L18 ANSWER 12 OF 25 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 91089769 MEDLINE
DOCUMENT NUMBER: 91089769 PubMed ID: 2264425
TITLE: Endotoxin, epinephrine, glucagon, insulin and calcium ionophore A23187 modulation of pyruvate kinase activity in cultured rat hepatocytes.
AUTHOR: Alston-Smith J; Ljungqvist O; Boija P O; Ware J; Ekdahl K N
CORPORATE SOURCE: Department of Clinical Immunology and Transfusion Medicine, University Hospital, Uppsala, Sweden.
SOURCE: ACTA CHIRURGICA SCANDINAVICA, (1990 Oct) 156 (10) 677-81.
Journal code: 7906530. ISSN: 0001-5482.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19910322

Entered Medline: 19910207

AB Altered ***glucose*** metabolism is one of the commonly observed sequelae of ***sepsis*** and septic shock. The present investigation was undertaken to determine the role of endotoxin (ET) upon hepatocyte glucoregulation, by measuring the activity of pyruvate kinase (PK), a key glycolytic enzyme. Hepatocytes were exposed to endotoxin concentrations known to occur in vivo during ***sepsis*** , i.e., from 1 X 10(-14) to 1 X 10(-8) g/ml. The alteration of the enzyme activities after addition of epinephrine, glucagon, ***insulin*** and calcium ionophore A23187 with and without ET preincubation were also examined. ET alone decreased the PK activity by 12% at all concentrations tested. The basal inhibition of the enzyme caused by epinephrine (-48%) was partially blocked by ET preincubation above 1 X 10(-10) g/ml. There were no ET-(glucagon, calcium ionophore, ***insulin***) interaction. These in vitro results do not support pyruvate kinase as a site of hepatic enzyme ***regulation*** defect in endotoxaemia.

L18 ANSWER 13 OF 25 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 91064928 MEDLINE
DOCUMENT NUMBER: 91064928 PubMed ID: 2174316
TITLE: Metabolic regulation of renal gluconeogenesis in response to sepsis in the rat.
AUTHOR: Ardawi M S; Khoja S M; Newsholme E A
CORPORATE SOURCE: Department of Clinical Biochemistry, College of Medicine and Allied Sciences, King Abdulaziz University, Jeddah, Saudi Arabia.
SOURCE: CLINICAL SCIENCE, (1990 Nov) 79 (5) 483-90.
Journal code: 7905731. ISSN: 0143-5221.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910308
Last Updated on STN: 19980206
Entered Medline: 19910117

AB 1. The ***regulation*** of renal gluconeogenesis was studied in rats made septic by a caecal ligation and puncture technique. 2. Blood ***glucose*** concentrations were not markedly different in septic rats, but lactate, pyruvate and alanine concentrations were markedly increased, compared with sham-operated rats. Conversely, blood ketone body concentrations were significantly decreased in septic rats. Both plasma ***insulin*** and glucagon concentrations were markedly elevated in response to ***sepsis*** . 3. The maximal activities of ***glucose*** -6-phosphatase (EC 3.1.3.9), fructose-1,6-bisphosphatase (EC 3.1.3.11), pyruvate carboxylase (EC 6.4.1.1) and phosphoenolpyruvate carboxykinase (EC 4.1.1.49) were markedly decreased in kidneys obtained from septic rats, suggesting diminished renal gluconeogenesis. 4. Renal concentrations of lactate, pyruvate and other gluconeogenetic intermediates were markedly elevated in septic rats, whereas those of acetyl-CoA and fructose 2,6-bisphosphate were decreased and unchanged, respectively. 5. The rate of gluconeogenesis from added lactate, pyruvate and glycerol was decreased in isolated incubated renal tubules from septic rats. 6. ***Sepsis*** decreased the arteriovenous concentration difference for ***glucose*** , lactate, and alanine. Septic rats showed decreased net rates of ***glucose*** production and net rates of removal of lactate and alanine as compared with sham-operated controls. 7. It is concluded that the diminished capacity for renal gluconeogenesis in septic rats could be the result of changes in the maximal activities or ***regulation*** of key non-equilibrium gluconeogenic enzymes or both, but the effect of other factors (e.g. toxins) has not been excluded.

L18 ANSWER 14 OF 25 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 90346019 MEDLINE
DOCUMENT NUMBER: 90346019 PubMed ID: 2200690
TITLE: Glucose tolerance and insulin secretion in experimental peritonitis in the rat.
AUTHOR: Andersson R; Pettersson M; Ahren B
CORPORATE SOURCE: Department of Surgery, Lund University, Sweden.
SOURCE: EUROPEAN SURGICAL RESEARCH, (1990) 22 (2) 101-12.
Journal code: 0174752. ISSN: 0014-312X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901026

Last Updated on STN: 19901026
Entered Medline: 19900917

AB The changes in the ***regulation*** of ***insulin*** secretion that accompany ***sepsis*** are yet to be fully established. We therefore examined ***insulin*** secretion both in vivo and in vitro in 2 different models of peritonitis/ ***sepsis*** in the rat. ***Sepsis*** was induced by intraperitoneal injection of Escherichia coli either alone or together with bile. Following ***sepsis*** induction, an initial hyperglycemia developed. This hyperglycemia was transient and had vanished after 3 h (coli group) or 9 h (bile group). However, after 24 h, a second phase of hyperglycemia developed in both groups. The ***glucose*** elimination rate after intravenous ***glucose*** injection (0.5 g/kg) at 4 and 10 h after peritonitis/ ***sepsis*** induction was retarded and the hyperglycemia that occurred during intravenous ***glucose*** infusion (10 mg/min for 30 min) was exaggerated. This is consistent with a reduced ***glucose*** uptake. Simultaneously, the plasma ***insulin*** responses to ***glucose*** were markedly exaggerated. This could be due to a true potentiated ***insulin*** secretion or simply to an adaptation to the hyperglycemia. However, also during intravenous arginine infusion (7 mg/min) at 4 h after peritonitis/ ***sepsis*** induction, the plasma ***insulin*** responses were markedly exaggerated. Since only a slight change in plasma ***glucose*** occurred during this challenge, the results suggest that ***sepsis*** is accompanied by a true hypersecretion of ***insulin*** . To verify whether this is directly or indirectly mediated, pancreatic islets were isolated from peritonitis/ ***sepsis*** animals at 4 h after disease induction and incubated for 45 min in a KRB medium supplemented with different concentrations of ***glucose*** . The subsequent ***insulin*** secretion was the same in islets from the septic animals as in controls. Hence, our results show that experimental peritonitis/ ***sepsis*** in the rat is accompanied by (1) ***glucose*** intolerance and (2) a true hypersecretion of ***insulin*** which is indirectly mediated.

L18 ANSWER 15 OF 25 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 89295149 MEDLINE
DOCUMENT NUMBER: 89295149 PubMed ID: 2661965
TITLE: Total and myofibrillar protein breakdown in different types of rat skeletal muscle: effects of sepsis and regulation by insulin.
AUTHOR: Hasselgren P O; James J H; Benson D W; Hall-Angeras M; Angeras U; Hiyama D T; Li S; Fischer J E
CORPORATE SOURCE: Department of Surgery, University of Cincinnati Medical Center, OH 45267.
CONTRACT NUMBER: 1RO1 DK37908-01 (NIDDK)
SOURCE: METABOLISM: CLINICAL AND EXPERIMENTAL, (1989 Jul) 38 (7) 634-40.
Journal code: 0375267. ISSN: 0026-0495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19970203
Entered Medline: 19890810

AB Proteolysis is increased in ***sepsis*** , but it is not known whether myofibrillar and non-myofibrillar proteins are broken down in the same fashion, or respond to the same ***regulatory*** forces as in non-septic muscle. In this study, therefore, the effect of ***sepsis*** on total and myofibrillar protein breakdown in incubated rat extensor digitorum longus (EDL) and soleus (SOL) muscles was determined, and the response in vitro to different concentrations of ***insulin*** (10 to 10(5) microU/mL) of protein degradation was studied in incubated EDL muscles from control and septic rats. ***Sepsis*** was induced in rats weighing 40 to 60 g by cecal ligation and puncture (CLP). Control animals were sham operated. Sixteen hours after CLP or sham operation, intact EDL and SOL muscles were incubated for two hours in oxygenated Krebs-Henseleit bicarbonate buffer containing ***glucose*** (10 mmol/L) and cycloheximide (0.5 mmol/L), and total and myofibrillar protein breakdown was assessed from release into incubation medium of tyrosine and 3-methylhistidine (3-MH), respectively. Tyrosine and 3-MH were determined fluorometrically by high performance liquid chromatography (HPLC). Tissue levels of tyrosine and 3-MH remained stable both in control and septic muscles during incubation for two hours. The rate of tyrosine release was increased during ***sepsis*** by 58% (P less than .001) and 15% (NS) in EDL and SOL muscle, respectively. The corresponding figures for 3-MH

were 103% (P less than .001) and 21% (NS). Tyrosine release was reduced by ***insulin*** at a concentration of 10(3) microU/mL in control muscle and at a concentration of 10(4) microU/mL in septic muscle.(ABSTRACT TRUNCATED AT 250 WORDS)

L18 ANSWER 16 OF 25 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 88297551 MEDLINE
DOCUMENT NUMBER: 88297551 PubMed ID: 2900204
TITLE: Clinical applications of somatostatin.
AUTHOR: del Pozo E
CORPORATE SOURCE: Experimental Therapeutics Department, Sandoz AG, Basle, Switzerland.
SOURCE: HORMONE RESEARCH, (1988) 29 (2-3) 89-91. Ref: 8
Journal code: 0366126. ISSN: 0301-0163.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880916

AB Because of its wide distribution in the organism, natural somatostatin (SRIF) demonstrates an ample spectrum of actions, involving mainly the central neuroendocrine system and the enteropancreatic area. In the former, this peptide may find its field of application in conditions characterized by excessive GH, TSH or ACTH secretion, depending on the central or peripheral cause of the inappropriate hormone control. The inhibitory effect of SRIF on gastrointestinal and pancreatic hormones may be useful in the management of tumors originating in this system and also in the treatment of inflammatory processes such as pancreatitis, in malignant diarrhea, and in gastrointestinal bleeding. A complex action of SRIF and its derivative on ***insulin*** release and ***glucose*** homeostasis may offer some advantages in the control of unstable diabetes. Dampening of organic functions in the upper digestive tract may also render SRIF and its analogues useful in the exploration of the gallbladder, gastric and pancreatic functions. The effect of such peptides on tissue growth and on the ***regulation*** of blood pressure are the subject of present investigations. Cytoprotection, an interesting aspect of SRIF application, is discussed elsewhere in this compendium. Finally, some comments on the possible use of SRIF as an additive to the conventional treatment of burns and ***sepsis*** close this review.

L18 ANSWER 17 OF 25 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 86308367 MEDLINE
DOCUMENT NUMBER: 86308367 PubMed ID: 3528546
TITLE: ***Regulation*** of ***glucose*** metabolism by altered pyruvate dehydrogenase activity. I. Potential site of ***insulin*** resistance in ***sepsis*** .
AUTHOR: Vary T C; Siegel J H; Nakatani T; Sato T; Aoyama H
CONTRACT NUMBER: GM 36139-01 (NIGMS)
SOURCE: JPEN. JOURNAL OF PARENTERAL AND ENTERAL NUTRITION, (1986 Jul-Aug) 10 (4) 351-5.
Journal code: 7804134. ISSN: 0148-6071.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19861001

AB Regulation of the pyruvate dehydrogenase (PDH) complex has been demonstrated to be a key mechanism in the control of carbohydrate oxidation and conservation of glucose carbon. The effect of sterile inflammation and chronic sepsis (small and large abscess) on the activity of the PDH complex was examined in liver and skeletal muscle. Sepsis altered the proportion of PDH in the active, dephosphorylated form. In hepatic tissue, sterile inflammation leads to a 2.5-fold increase in the proportion of active PDH complex compared to fed control. The same increase in the proportion of active PDH complex was observed in rats with a small septic abscess. However, when the severity of septic episode was increased, the proportion of active PDH complex decreased relative to sterile inflammation or small septic abscess animals. A different pattern

in the response to sterile inflammation and sepsis on the proportion of active PDH complex was observed in skeletal muscle compared to liver. In contrast to liver, sterile inflammation did not alter the proportion of active PDH in skeletal muscle. In addition, sepsis (either small or large septic abscess) resulted in a 3-fold decrease in the proportion of active PDH relative to fed control or sterile inflammatory animals. The decrease in the proportion of active PDH complex in sepsis was associated with a corresponding increase in the skeletal muscle acetyl-CoA/CoA ratio. The mechanism responsible for lowered PDH complex activity may have been due to increased PDH kinase activity, secondary to increased skeletal muscle acetyl-CoA/CoA ratios.

L18 ANSWER 18 OF 25 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 85102144 MEDLINE
DOCUMENT NUMBER: 85102144 PubMed ID: 3881289
TITLE: Monokines and the metabolic pathophysiology of septic shock.
AUTHOR: Filkins J P
CONTRACT NUMBER: GM 29619 (NIGMS)
SOURCE: FEDERATION PROCEEDINGS, (1985 Feb) 44 (2) 300-4. Ref: 46
Journal code: 0372771. ISSN: 0014-9446.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198503
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850318

AB The role of the macrophage system in shock pathogenesis now embraces both classic endocytic functions as well as the more recently discovered function of the macrophages as a multifaceted secretory apparatus. Among the major macrophage secretory products are the monokines, ***regulatory*** proteins that mediate via both local or paracrine and systemic or endocrine mechanisms, the nonspecific host defense and metabolic responses to inflammation and ***sepsis*** . Evidence is reviewed for a monokine involvement in the alterations of protein, fat, and carbohydrate metabolism in ***sepsis*** and/or endotoxicosis, viz., enhanced muscle proteolysis, enhanced hepatic acute phase protein synthesis, depressed lipogenesis and lipoprotein lipase function, enhanced peripheral ***glucose*** oxidation, and depression of hepatic gluconeogenesis. Monokines are also related to the disturbed endocrine mechanisms of ***sepsis*** , viz., enhanced ***insulin*** secretion and depressed adrenal steroidogenesis. It is suggested that the macrophage system mediates via secretion of monokines an integrated fuel substrate and hormonal adjustment to ***sepsis*** , which on the one hand may provide optimal metabolic homeostasis for systemic host defense, but on the other hand, if allowed to act unchecked, may contribute to the metabolic dyshomeostasis of septic shock.

L18 ANSWER 19 OF 25 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 85012039 MEDLINE
DOCUMENT NUMBER: 85012039 PubMed ID: 6384722
TITLE: Carbohydrate dynamics in the hypermetabolic septic rat.
AUTHOR: Lang C H; Bagby G J; Spitzer J J
CONTRACT NUMBER: GM 07029 (NIGMS)
GM 32371 (NIGMS)
SOURCE: METABOLISM: CLINICAL AND EXPERIMENTAL, (1984 Oct) 33 (10) 959-63.
Journal code: 0375267. ISSN: 0026-0495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198411
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19841109

AB ***Glucose*** turnover is increased during shock and in acute ***sepsis*** , but relatively little information is available concerning the ***regulation*** of carbohydrate metabolism during the hypermetabolic phase of ***sepsis*** . In these studies peritoneal ***sepsis*** was induced in rats, following chronic vascular catheterization, by intraperitoneal administration of a pooled fecal inoculum. The resultant peritonitis has been shown to produce a sustained hypermetabolic state during the first three days of infection.

glucose and lactate kinetics were studied using a constant infusion of radiolabeled tracers during the peak of the hypermetabolic phase (day 2). The septic animals exhibited a 42% increase in ***glucose*** turnover and a 63% increase in the metabolic clearance rate of ***glucose*** , as compared to time-matched control rats. Hepatic glycogenolysis could only contribute 1% to 2% to the increased rate of ***glucose*** appearance. A major portion of the elevated ***glucose*** turnover was accounted for by a 93% increase in ***glucose*** recycling, indicating an enhancement of gluconeogenesis from ***glucose*** -derived gluconeogenic precursors. The increased importance of lactate as a precursor for gluconeogenesis in ***sepsis*** was indicated by the elevated lactate turnover (34%) and the increased percentage of 14C- ***glucose*** derived from 14C-lactate. The ***insulin*** to glucagon ratio was decreased in the septic animals as a result of a reduction in the plasma ***insulin*** concentration (56%) and an increased glucagon concentration (67%). We conclude that during the hypermetabolic phase of ***sepsis*** , the increased peripheral ***glucose*** uptake generated more gluconeogenic precursors but did not appear to have a major direct contribution to the increased aerobic metabolism.

L18 ANSWER 20 OF 25 MEDLINE
ACCESSION NUMBER: 85097254 MEDLINE
DOCUMENT NUMBER: 85097254 PubMed ID: 6394000
TITLE: Reticuloendothelial system function and glucose-insulin dyshomeostasis in sepsis.
AUTHOR: Filkins J P
CONTRACT NUMBER: HL 08682 (NHLBI)
SOURCE: AMERICAN JOURNAL OF EMERGENCY MEDICINE, (1984 Jan) 2 (1) 70-3.
Journal code: 8309942. ISSN: 0735-6757.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198503
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850321

AB Circulating ***glucose*** levels, peripheral ***glucose*** utilization, and hepatic gluconeogenesis were compared in late endotoxicosis and severe septic shock in rats. Endotoxin was administered intravenously as 5 mg of Salmonella enteritidis lipopolysaccharide B. ***Sepsis*** was induced in the peritoneal cavity by use of the cecal ligation and puncture technique. Late endotoxicosis and severe ***sepsis*** were comparable in hypoglycemia, increased peripheral ***glucose*** use, and depression of gluconeogenesis. Immunoreactive ***insulin*** was lower in endotoxicosis than in ***sepsis*** ; both models demonstrated elevations in serum nonsuppressible ***insulin*** -like activity. Endotoxic pancreata secreted excessive ***insulin*** , as did pancreata obtained after blockade of the reticuloendothelial system (RES). Macrophage-conditioned media induced a hypersecretory state of the beta cells in donor pancreata. The RES serves as a source of secretory products, i.e., gluco- ***regulatory*** monokines, which affects insulinization of tissues in ***sepsis*** and thus underwrites the hypoglycemia of late endotoxicosis and severe ***sepsis*** .

L18 ANSWER 21 OF 25 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 85025325 MEDLINE
DOCUMENT NUMBER: 85025325 PubMed ID: 6149025
TITLE: Energy and substrate kinetics and oxidation during ketone infusion in septic dogs: role of changes in insulin and glucagon.
AUTHOR: Shaw J H; Wolfe R R
CONTRACT NUMBER: GM00455-05 (NIGMS)
SOURCE: CIRCULATORY SHOCK, (1984) 14 (1) 63-79.
Journal code: 0414112. ISSN: 0092-6213.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198412
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19841219

AB We have investigated the response of ***glucose*** and free fatty acid (FFA) kinetics and oxidation to betahydroxybutyrate (BOHB) infusion (30

mumol/kg X min) in both normal and Escherichia coli septicemic conscious dogs. In both the septic and control groups, experiments were performed in which hormone levels were allowed to change in response to the BOHB infusion, and in which the infusion of somatostatin, ***insulin*** , and glucagon were used to hold those hormone levels constant and sympathetic activity was blocked by the infusion of propranolol and phentolamine. In the nonseptic groups, the infusion of BOHB decreased both ***glucose*** production and FFA appearance (RaFFA) independent of the hormonal status. ***Glucose*** oxidation decreased in proportion to the decrease in production and uptake. FFA oxidation decreased only when hormones were controlled. In contrast, the infusion of BOHB in septic dogs did not suppress either ***glucose*** production or RaFFa, irrespective of the hormonal status. Substrate oxidation again corresponded to the rate of appearance of the substrate. We conclude that in normal dogs, ketones act directly as metabolic ***regulators*** to decrease the appearance of both ***glucose*** and FFA in the plasma, but do not directly affect the ability of the animal to oxidize these substrates. In ***sepsis*** , the normal ***regulatory*** actions of ketones appear to be lost.

L18 ANSWER 22 OF 25 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 83031516 MEDLINE
DOCUMENT NUMBER: 83031516 PubMed ID: 6752238
TITLE: Hormonal changes and their influence on metabolism and nutrition in the critically ill.
AUTHOR: Dahn M S; Lange P
SOURCE: INTENSIVE CARE MEDICINE, (1982) 8 (5) 209-13. Ref: 39
Journal code: 7704851. ISSN: 0342-4642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198212
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19821221

AB This is a brief review of the observed hormonal alterations following trauma and ***sepsis*** . The major changes noted in the metabolic status of the stressed patient have been characterized by deranged carbohydrate metabolism, altered metabolic rate as measured by oxygen consumption and increased ureagenesis. Each of these phenomena are ***regulated*** to a large extent by the specific hormonal profile of the patient. Failure of ***insulin*** and growth hormone production have been associated with ***glucose*** intolerance, excessive urinary nitrogen loss and a fatal outcome. Glucagon, cortisol and catecholamines exhibit sustained elevation and have been associated with increased metabolic rate and excessive ureagenesis. These changes are usually self limited following trauma but will persist if the patient enters a septic phase. The use of specific nutritional support, namely hypertonic ***glucose*** versus a balanced fat emulsion system in the face of ***sepsis*** is considered.

L18 ANSWER 23 OF 25 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 82055671 MEDLINE
DOCUMENT NUMBER: 82055671 PubMed ID: 7029002
TITLE: Glucose-dependent changes in growth hormone regulation associated with sepsis.
AUTHOR: Kirkpatrick J R; Dahn M
SOURCE: JOURNAL OF TRAUMA, (1981 Nov) 21 (11) 925-30.
Journal code: 0376373. ISSN: 0022-5282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198201
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19820120

AB Major alterations in the ***glucose*** -mediated ***regulation*** of growth hormone are associated with ***sepsis*** ; however, these alterations are not related to the rate of change in plasma ***glucose*** or changes in glucagon, epinephrine levels, or circulating levels of arginine. Alterations in the growth hormone ***regulatory*** mechanism occurred among septic patients who manifested severe ***glucose*** intolerance which was associated with suppression of ***insulin*** production. Inhibition of growth hormone release in these

patients may have an adverse effect on amino acid movement, which lends further support to the concept that sustained hyperglycemia in the septic patient is undesirable.

L18 ANSWER 24 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 82039456 EMBASE
DOCUMENT NUMBER: 1982039456
TITLE: Glucose-dependent changes in growth hormone regulation associated with sepsis.
AUTHOR: Kirkptrick J.R.; Dahn M.
CORPORATE SOURCE: Dept. Surg., Wayne State Univ. Sch. Med., Detroit, MI 48201, United States
SOURCE: Journal of Trauma, (1981) 21/11 (925-930).
CODEN: JOTRA5
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology
006 Internal Medicine
009 Surgery
004 Microbiology
LANGUAGE: English
AB Major alterations in the ***glucose*** -mediated ***regulation*** of growth hormone are associated with ***sepsis*** ; however, these alterations are not related to the rate of change in plasma ***glucose*** or changes in glucagon, epinephrine levels, or circulating levels of arginine. Alterations in the growth hormone ***regulatory*** mechanism occurred among septic patients who manifested severe ***glucose*** intolerance which was associated with suppression of ***insulin*** production. Inhibition of growth hormone release in these patients may have an adverse effect on amino acid movement, which lends further support to the concept that sustained hyperglycemia in the septic patients is undesirable.

L18 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:111959 CAPLUS
DOCUMENT NUMBER: 68:111959
TITLE: Action of epinephrine and other hormones associated with the stress response on potassium movement, with special reference to the development of postoperative depletion states
AUTHOR(S): Shoemaker, William C.
CORPORATE SOURCE: Cook County Hosp., Chicago, IL, USA
SOURCE: Review of Surgery (1968), 25(1), 9-24
CODEN: RESUAR; ISSN: 0034-6780
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The response of specific hormones known to be operative in trauma or known to exert metabolic actions similar to those assocd. with trauma were studied using methods for measuring organ blood flow and organ metabolism under controlled exptl. conditions in the unanesthetized dogs. Epineprine, administered by vena caval injection of 1-10 .gamma./kg., produced increased arterial pressure and hepatic blood flow; the latter consisted of increased portal venous flow, initially decreased hepatic arterial flow, and increased resistance across the hepatic arterial tree, but not across the portal venous circuit. The intraportal injection of epinephrine increased portal venous resistance of hepatic vasculature. Small doses of epinephrine and glucagon caused increased hepatic K+ output which preceded the hemodynamic and metabolic effects of these hormones. The epinephrine-stimulated hepatic K+ output was followed by increased hepatic ***glucose*** output and increased hepatic uptake of lactate, pyruvate, and amino acids. K+ release in the perfused liver after epinephrine was assocd. with HCO3- and Cl- output as well as uptake of Na+ and H+ or its equiv. Hepatic K+ release occurred in controlled exptl. conditions where animals had been subjected to shock from hemorrhage and thermal injury. The hepatic K+ efflux preceded the activation of hepatic phosphorylase in the intact animal. Glucagon, norepinephrine, and cortisol also increased hepatic K+ release; by contrast, ***insulin*** administration increased hepatic K+ removal from the plasma. K+ abnormalities led to some fluid electrolyte problems in severe stress states and were also assocd. with excessive metabolic demands from trauma, multiple complications, prolonged febrile states, ***sepsis*** , stormy convalescence, inadequate supply of nutritional requirements during prolonged parenteral feeding, and other types of inadequate caloric intake. The nature and genesis of fluid electrolyte changes which occurred after trauma were reviewed. The relation of electrolyte movements to hemodymamic and metabolic changes and the manner by which

these interrelations might be ***regulated*** by hormonal actions were discussed. 29 references.

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     (FILE 'HOME' ENTERED AT 17:12:00 ON 14 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     17:12:21 ON 14 JUL 2003
L1           32 S CRITICALLY ILL POLYNEUROPATHY
L2        28756 S POLYNEUROPATHY
L3          178 S GLUCOSE REGULATOR
L4            1 S L2 (P) L3
L5       900162 S INSULIN
L6            0 S L5 (P) L1
L7          626 S L5 (P) L2
L8           14 S L7 (P) GLUCOSE (P) REGULAT?
L9            6 DUPLICATE REMOVE L8 (8 DUPLICATES REMOVED)
L10           6 S L9 NOT L4
L11        4562 S SYSTEMIC INFLAMMATORY RESPONSE SYNDROME
L12        3926 S SIRS
L13        6511 S L11 OR L12
L14      135459 S SEPSIS
L15        1454 S (L13 OR L14) (P) L5
L16           0 S L15 (P) GLUCOE (P) REGULAT?
L17          71 S L15 (P) GLUCOSE (P) REGULAT?
L18          25 DUPLICATE REMOVE L17 (46 DUPLICATES REMOVED)

=> s van den berghe greta/au
L19           1 VAN DEN BERGHE GRETA/AU

=> d l19 1 ibib abs

L19  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:833142  CAPLUS
DOCUMENT NUMBER:          135:353239
TITLE:                    Critical illness neuropathy treatment with blood
                          glucose regulators
INVENTOR(S):                ***Van Den Berghe, Greta***
PATENT ASSIGNEE(S):       Novo Nordisk A/S, Den.; K.U. Leuven R + D
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       --------------    --------
     WO 2001085256      A2   20011115       WO 2001-DK287     20010430
     WO 2001085256      A3   20020221
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             CR, CU, CZ, DE, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2001054621      A5   20011120       AU 2001-54621     20010430
     EP 1292324         A2   20030319       EP 2001-927641    20010430
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2002107178      A1   20020808       US 2001-853193    20010511
PRIORITY APPLN. INFO.:                     GB 2000-10856     A  20000505
                                           DK 2001-604       A  20010415
                                           DK 2001-605       A  20010416
                                           WO 2001-DK287     W  20010430
AB   This invention relates to a life saving medicament for critically ill
     patients and a method of treatment.  The compn. is a pharmaceutically
     effective amt. of a blood glucose regulator which is used to control the
     blood glucose level.  An examples is given of a clin. study in which the
     hypothesis that the incidence of crit. illness neuropathy can be reduced
     by more strict metab. using intensive insulin treatment from admission
     onward.
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     (FILE 'HOME' ENTERED AT 17:12:00 ON 14 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     17:12:21 ON 14 JUL 2003
L1            32 S CRITICALLY ILL POLYNEUROPATHY
L2         28756 S POLYNEUROPATHY
L3           178 S GLUCOSE REGULATOR
L4             1 S L2 (P) L3
L5        900162 S INSULIN
L6             0 S L5 (P) L1
L7           626 S L5 (P) L2
L8            14 S L7 (P) GLUCOSE (P) REGULAT?
L9             6 DUPLICATE REMOVE L8 (8 DUPLICATES REMOVED)
L10            6 S L9 NOT L4
L11         4562 S SYSTEMIC INFLAMMATORY RESPONSE SYNDROME
L12         3926 S SIRS
L13         6511 S L11 OR L12
L14       135459 S SEPSIS
L15         1454 S (L13 OR L14) (P) L5
L16            0 S L15 (P) GLUCOE (P) REGULAT?
L17           71 S L15 (P) GLUCOSE (P) REGULAT?
L18           25 DUPLICATE REMOVE L17 (46 DUPLICATES REMOVED)
L19            1 S VAN DEN BERGHE GRETA/AU

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                68.14      68.35

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -1.95      -1.95

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